

STRUEH (C.)

# ONCE MORE ON ANTITOXIN.

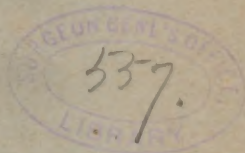
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BY CARL STRUEH, M.D.  
CHICAGO.

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REPRINTED FROM THE  
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION,  
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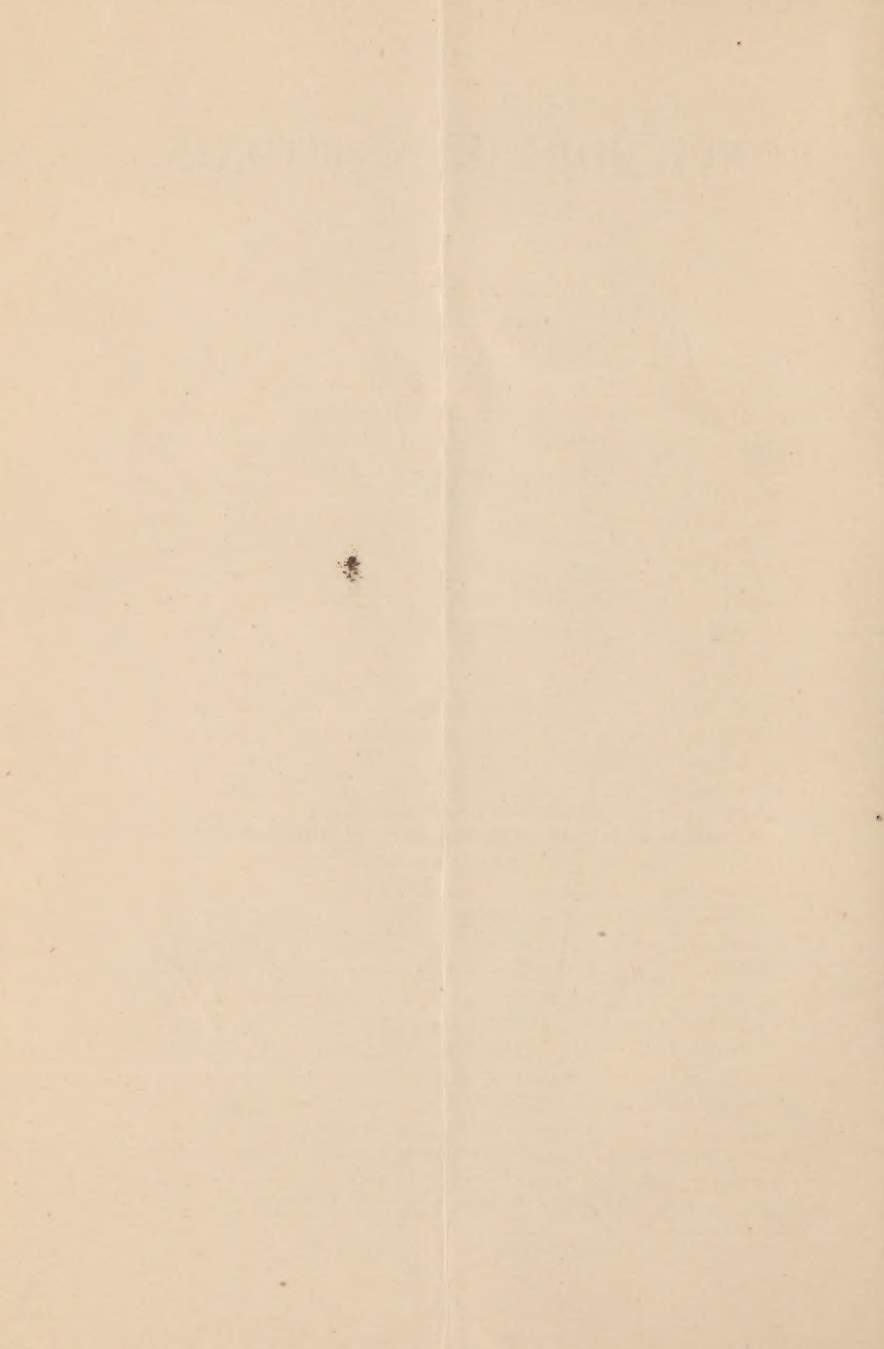
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## ONCE MORE ON ANTITOXIN.

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In the issue of the JOURNAL of January 25 of the current year, there appeared a short article of mine entitled "Criticism of the Antitoxin Treatment from a Different Standpoint," in regard to which I received a very interesting letter from my friend Dr. X. at St. P., in which letter the doctor opposes in a most instructive manner some remarks which I have made in my article. As Dr. X. apparently represents the opinion of the majority of the advocates of the antitoxin treatment, I am very much indebted to him for giving me the permission to discuss the contents of his letter in the JOURNAL.

Dr. X., in short, says: 1, that the statistics we have, at the present time, command of are made from such cases which were proven to be diphtheria from a bacteriologic examination, and that these statistics in comparison with those we had under the old treatment are so much in favor of the antitoxin that we must ascribe the lower mortality to the latter; 2, that he believes in the efficacy of the drugs for local and general treatment, so that he does not think the exclusion of the drug treatment is the cause of the lower mortality; 3, that he has seen most surprising changes in the course of the disease, which changes he could only ascribe to the serum treatment; 4, that he has never seen any ill effects from the antitoxin; 5, that he saw some recoveries from croup under the serum treatment without intubation or tracheotomy having been required; 6, that he does not agree with my saying that "it is not the rule that from a child being sick with diphtheria the majority of the family becomes infected," and he believes that by immunization many a child can be protected against diph-



theria; 7, that he believes we will have a serotherapy for typhoid in the future as we have for diphtheria now.

I am well aware that it is not an easy task to successfully contradict these statements. Still we will see what can be said against them.

In regard to the first statement I fully admit that we possess quite a number of statistics which give very much credit to the antitoxin. I undertook to inquire about the death rate with the serum treatment from the health commissioners of different cities in the United States, and received a great number of statistics, some of which show the following figures:

#### NEW YORK CITY.

Diphtheria and croup; case fatality, first, second and third quarters of each year, 1891 to 1895 inclusive:

Year.	Cases.	Deaths.	Percentage.
1891	3,686	1,349	36.59
1892	4,158	1,540	37.04
1893	4,721	1,763	37.34
1894	7,446	2,284	30.67
1891-4	20,011	6,936	34.66
1895	7,921	1,543	19.43

Reduction in death rate first second and third quarters of 1895, as compared with average death rate for corresponding periods of previous four years, 16.23 per cent., or a reduction of 43.94 per cent. of the previous rate.

Case fatality, fourth quarters of 1891 to 1893 inclusive, and 1895.

Year.	Cases.	Deaths.	Percentage.
1891	1,678	621	37.01
1892	1,126	566	50.26
1893	2,400	795	33.13
1891-3	5,204	1,982	40.13
1895	2,465	433	17.52

Reduction of death rate, fourth quarter of 1895, as compared with average death rate for corresponding periods of the years 1891-1893 is 22.61 per cent. or a reduction of 56.34 per cent. of the previous rate.

Table showing case fatality in diphtheria and croup in New York city for the period Jan. 1, 1895, to Oct. 6, 1895 (during which antitoxin was employed), as compared with the period between Jan. 1, 1894, and Oct. 6, 1894. The figures denote the percentage in periods of four weeks.

	1894	1895	1896
January 27 . . . . .	43.30	25.77	
February 24 . . . . .	39.43	24.43	
March 24 . . . . .	34.20	20.31	
April 21 . . . . .	36.00	20.68	
May 19 . . . . .	35.96	20.76	
June 16 . . . . .	30.50	20.58	
July 14 . . . . .	27.06	12.23	
August 11 . . . . .	30.51	19.63	
September 8 . . . . .	33.15	23.74	
October 6 . . . . .	29.76	18.93	
November 2 . . . . .		16.66	
November 30 . . . . .		21.02	
December 28 . . . . .		16.32	
January 25 . . . . .			15.97
Total cases . . . . .	6,876	7,475	3,373
Total deaths . . . . .	2,337	1,582	580
Average case fatality..	33.93	21.16	

#### INDIANAPOLIS.

Report for the seven months ending Jan. 31, 1896.  
Before using antitoxin:

1895	Cases.	Deaths.
July . . . . .	4	3
August . . . . .	26	6
September . . . . .	70	27
October . . . . .	132	25
Total . . . . .	232	61

Showing the per cent. of deaths to the number of cases to be 26.29 in a hundred.

After using antitoxin:

	Cases.	Deaths.
November, 1895 . . . . .	93	10
December, 1895 . . . . .	65	12
January, 1896 . . . . .	44	5
Total . . . . .	202	27

Showing a death rate of 13.36 per cent. to the hundred cases.

#### ST. LOUIS.

In the first six months of 1895 there were reported to the health office 645 cases of diphtheria of which 164 proved fatal, which was a mortality of 25.4 per cent. In the last six months of 1895 there were reported 2,233 cases, of which 355 proved fatal, which was a mortality of 15.8 per cent. The record of diphtheria in St. Louis for the past ten years is as follows:

Year.	Cases.	Deaths.	Per-centage.
1886 . . . . .	2,826	719	25.44
1887. . . . .	3,108	927	29.82
1888. . . . .	1,658	564	34.01
1889. . . . .	1,240	345	27.82
1890. . . . .	667	185	27.73
1891. . . . .	771	249	32.29
1892. . . . .	671	208	31.00
1893. . . . .	613	242	39.47
1894. . . . .	751	238	31.69
1895. . . . .	2,878	519	18.03
Total. . . . .	15,186	4,196	

#### MINNEAPOLIS.

The total number of cases reported in 1895 was 569, with 114 deaths (mortality 20 per cent.). In 131 cases antitoxin was used, with 11 deaths (mortality 8.4 per cent.). The previous year the total number of cases was 191, with 54 deaths (mortality 28.2 per cent.).

Statistics similarly favorable are reported from a large number of places where antitoxin has been used. And yet I doubt that these reports, even if they were all unobjectionable as such, are appropriate evidence already for deciding definitely, as a great number of physicians do, upon a question of such comprehensive signification. In the first place, we must not forget that statistics as such are most unreliable, because every individual case differs from others so that we always compare unequal values. Furthermore, en-



demic, epidemic and other circumstances cut such a figure that it at the least seems very risky to decide upon the value of a new remedy from the experience of one or a few years. In the Children's Hospital at Basel, for instance, the mortality in 1876 was 34 per cent., in 1886 only 6 per cent. Had they used any new remedy during the latter year, the decrease in the mortality would undoubtedly have been ascribed to the new treatment.

How much the statistic results of the serumtherapy must depend upon other influences we learn from the difference in the mortality, which various observers claim, as is shown in the following percentage figures:

Stockholm 2, Holland 7, Minneapolis 8.4, Chicago, 8.93, Paris Children's Hospital (Lebreton and Magdelaine, 330 cases) 12, Rumpf 12, Ganghofer 12.72, Baginsky 13, France 13, Indianapolis 13, Bokai 14, Washburn 14, Hungary 14.3, Italy 14.4, Soltmann 14.6, Germany 14.8, Austria 14.9, St. Louis 15, Berlin 17.4, New York City 19, Constantini 22, Vienna 22.8, Kossel 23, England 23, Widerhofer 24, Roux, Martin, Chaillou 26; Milwaukee 27, Waingen 28, Körte in grave cases 58.2, medium 29.8, light 3.3, Gnändinger 40, Trieste (252 cases) 63.

So we see that the mortality ranges from 2 per cent. to 63 per cent., a difference hardly possible if the treatment were a "specific." There are other reports from which we learn that the difference in the mortality before and after the use of antitoxin does not at all give proof of the value of the serum. The Friedrichshain statistics, for instance, show the following mortality:

1888, 32 per cent.; 1889, 34 per cent.; 1891, 1892, 1893, 38 per cent.; 1894 (February to November, serum period), 33 per cent.

So in 1888, when no antitoxin was used, the mortality was lower than during the serum period in 1894.

I note the same feature in the Milwaukee statistics. In 1891 the death rate is lower than during the serum period in 1895.

## MILWAUKEE.

Year.	Cases.	Deaths.	Per-centage.
1890 . . . . .	827	241	29.13
1891 . . . . .	1,489	400	26.79
1892 . . . . .	1,193	400	33.53
1893 . . . . .	620	209	33.71
1894 . . . . .	436	175	40.13
Total. . . . .	4,565	1,425	31.19
February, 1895 <sup>1</sup> . . . . .	433	117	27.02

Very important are the statistics which show the actual number of deaths from diphtheria and croup in the city of Berlin, viz.:

1881, 1,953; 1882, 1,913; 1883 (severe epidemic), 2,561; 1884 (severe epidemic), 2,446; 1885, 1,802; 1886, 1,535; 1887, 1,304; 1888, 1,070; 1889, 1,252; 1890, 1,549; 1891, 1,057; 1892, 1,405; 1893 (serum period), 1,643; 1894 (serum period), 1,430.

This table shows that the antitoxin did not cause any decrease in the actual number of deaths from diphtheria whatever, even allowing for the increase in population.

There are also reports which show an equal or even lower death rate by the use of other treatments than is claimed for the antitoxin treatment. So in Basel the average mortality in 4,479 cases which were treated during 17 years, was 12.6 per cent.

Dr. S. Schwarz, of Constantinople, recommends treating diphtheria by insufflations of sozodol-sodium and flowers of sulphur, besides giving for internal use chlorate of potassium (15.22 gr. :3vi, a tablespoonful every hour) and ext. of nux vomica (2 to 3 times daily) right from the beginning of the disease in order to prevent post-diphtheritic paralysis. Under this treatment he claims to have a mortality of 8 to 10 per cent. and only 2 to 3 per cent. (!) if the cases come under treatment at an early stage. (*Wiener medicinische Wochenschrift*, 1895, No. 43.) I should think that without this nefarious treatment the death rate would have been considerably lower.

Dr. N. Rosenthal, of Berlin, reports 271 cases which

<sup>1</sup> The month in which antitoxin commenced to be used in Milwaukee.

were treated (locally and generally) with sol. of sesquichlorid of iron, a mortality of 8.2 per cent. resulting. (*Therapeutische Monatshefte*, 1895, No. 11.) On the other hand we possess reports showing an increased mortality under the serum treatment. The *Lancet* of Oct. 26, 1895, states that "the mortality from diphtheria in London was more than 40 per cent. in excess of the corrected average for the fortieth week of the last decennial period," in spite of the antitoxin. We also must consider that those statistics which are so much in favor of the serum treatment, are not all unobjectionable. In regard to the statistics of Behring, the main representative of the serum-therapy, for instance, I refer to an article, Serum-therapy and Statistics by Dr. A. Gottstein, Berlin, which appeared in the *Therapeutische Monatshefte*, 1895, No. 11, and in which Behring's statistics is criticized in a very illucidating way by Gottstein presenting authentic figures which were furnished by the Royal Health Department of Berlin, and which relate to all Berlin hospitals and to all cases which were reported by local physicians, so that these figures represent a collective statistic of all Berlin. According to Gottstein the lower mortality must in a great measure be ascribed to the fact that since the introduction of the serum-therapy almost twice as many cases were reported as before, so that Behring does not go by the real number of cases which occurred, but by the number reported. Since 1884 there is existing in Berlin an ordinance making it obligatory for physicians to report diphtheria cases, and in 1887 disinfection was made compulsory. Everybody who knows to what inconveniences the general practitioner subjects his patients and himself in complying with these two ordinances, will understand that perhaps the majority of the physicians ceased to report all of their cases, that in other words the number of reports decreased.

In 1894, two Berlin physicians were indicted for not having reported diphtheria, and the state's attor-

ney motioned for punishment by imprisonment, a circumstance which caused a rapid increase of the reports. Behring's own table shows this fact. There were reported:

	1st Quarter.	2d Quarter.	3d Quarter.	4th Quarter.
1889 . . .	978	945	1,075	1,243
1890 . . .	1,120	1,019	1,136	1,237
1891 . . .	830	763	763	1,086
1892 . . .	879	822	875	1,267
1893 . . .	1,027	962	1,107	1,275
1894 . . .	1,114	1,085	1,058	2,028

So the fourth quarter of the year 1894 shows almost a duplication of the number of cases which were reported. Or does Behring believe that twice as many cases occurred? "If he does," says Gottstein, "we can claim with the same right that the introduction of the serum-therapy was the cause of the increase of diphtheria."

If, however, twice as many cases were reported as before, it is not surprising that the death rate decreased for the figures undoubtedly include many mild cases which previously were not reported.

A statistic which, it seems to me, does not carry much weight, is the one which emanates from our Chicago Health Department and which I find reported in the periodical *The Clinique*, 1895, February 15, No. 11. It is stated in this statistic that since the introduction of the serum-therapy the mortality has decreased from about 52 per cent. to less than 9 per cent., a change which we should all welcome with delight were it not for the fact that the compilers of this report compared a statistic of 1,047 cases treated with antitoxin to one of only 61 cases treated without it. Such a report is absolutely worthless, for the reason that comparative statistics should always relate to an almost equal number of cases. Besides the report fails to enlighten us as to what (drug) treatment was employed in the sixty-one cases.

I was very much surprised when in a Chicago daily paper I read an article which was written in commendation of the serum treatment and in which all the



figures favorable to antitoxin were given as I find them recorded by the health department, that no mention at all was made of those sixty-one cases to which the 52 per cent. relate. The statistic as I find it in *The Clinique* is as follows:

Total number of cases of diphtheria visited . . . . .	1,221
At request of attending physician . . . . .	1,169
Charity patients (no physician in attendance) . . . . .	52
Total number found convalescent on arrival . . . . .	68
Total number found dead on arrival . . . . .	50
All other cases . . . . .	1,108
Total number suffering from diphtheria . . . . .	1,108
Total number treated with antitoxin . . . . .	1,047
Total number in which antitoxin was not used . . . . .	61
Total number recovered under antitoxin treatment . . . . .	961
Total number died under antitoxin treatment . . . . .	85
Death rate under antitoxin treatment 8.98 per cent.	
Total number in which antitoxin was not used . . . . .	61
Total number of these known to have died . . . . .	32
Death rate when antitoxin was not used 52.46 per cent. <sup>2</sup>	

A statistic similar to that of Chicago was some time ago reported from Boston, where the mortality was said to have decreased from about 50 to 16 per cent. the latter relating to sixty-nine cases of which eleven died, quite a good percentage for a "specific." If I should lose every sixth patient I would hardly feel as though I had a specific. From the few statistics I have cited as examples, we see that they are so contradictory, objectionable and depending upon other influences that we certainly can not yet rely upon them very much. We must also consider that when a new remedy has once gained favor, in the first flood of enthusiasm those practitioners having favorable results are always more anxious to report their cases than those having unfavorable ones. And yet one of the latter amounts to more than ten of the former, because it shows the limits of the efficacy of the treatment. Even those unfavorable reports already existing are not sufficiently considered by the antitoxin enthused physicians. We must, therefore, extend our observations over a greater length of time and

<sup>2</sup> "Not used" either because the case was hopeless when seen (!); or the administrator feared the result of its use—as, for example, on the fourth day or later, or because the family or the attending physician changed attitude after calling on the department and refused its use. I should not think they would declare a case hopeless until they used their "specific," especially if it is, as they claim, harmless.

wait for other epidemics, before we can form a definite opinion, as far as the statistics are concerned, if we insist on laying so much weight on them.

I personally believe that the mortality has decreased under the antitoxin treatment, but I largely ascribe this decrease to the exclusion of the drug treatment, as also good results were obtained in the tuberculin treatment after creosote had been excluded.

The report from the Kaiser and Kaiserin Hospital at Berlin seems to support this assertion. "The average mortality in this hospital was in the neighborhood of 50 per cent. before the use of antitoxin, but upon its introduction the death rate was reduced to below 10 per cent. Then during two months (July and August) the supply of serum having failed, the death rate rose to the former general average, again to fall to the low rate upon the renewal of the antitoxin treatment."

This report deserves consideration in so far as we can exclude endemic conditions as being the cause of the decrease of the death rate. It would, however, be very interesting to know what local and general treatment they used before the introduction of the antitoxin treatment and at the time, when the supply of serum failed. They certainly did not leave the cases without any treatment. If it was the old drug treatment, we can easily explain the fluctuation in the mortality. Even Virchow who was made an advocate of the serum therapy by these "brutal figures," does not seem to have taken into consideration the effect of the interim treatment. It seems to me that the average practitioner does not sufficiently consider the harmfulness of the drug treatment, for we often hear a physician say that he used no other treatment besides the antitoxin and that he obtained splendid results, which, therefore, in his opinion could only be ascribed to the serum. I think quite differently; just because he had not used any other treatment, he had such good results. Again, there are physicians who use antitoxin with their entire former treatment and claim to

have obtained better results than before. But this does not prove much either, as apparent good results can be obtained even by a harmful treatment, if the endemic, epidemic and other conditions are favorable, as we see, for instance, from the report of Dr. Schwarz to which I have previously referred. Still I find as a rule that the drug treatment is either entirely excluded or applied in a modified form, when antitoxin is being used. This brings us to statement No. 2 concerning the drug treatment. First I wish to say a few words in regard to the local treatment which is mainly based upon the principle of antiseptics and which is carried out by the following five manipulations: Gargling, spraying, insufflating, swabbing and cauterizing. Now, supposed, but not admitted, that the bacilli diphtheriae were the main part in the disease, and supposed that these bacilli were not burrowed in the mucous membrane, but were located right upon the diphtheritic membrane and could easily be reached by our manipulations, I do not understand what effect these manipulations could have. We know, and this has been proven by experiments, that a bacillus must be exposed to an antiseptic solution of a certain concentration for a certain length of time in order to be destroyed. If the antiseptic solution is not of the necessary strength or if the bacillus is not exposed to the antiseptic for the necessary length of time, our efforts toward destroying the bacillus will be futile. I refer to Sternberg's manual of bacteriology (1893), in which he gives extensive tables of the effects of different antiseptic solutions upon the various bacilli.

We must also consider that a far stronger solution than is required to kill bacilli will be necessary to destroy the spores. We must also consider that in presence of organic material in association with bacteria the disinfectant can be neutralized before the living bacteria are destroyed. For instance, the cholera bacillus in bouillon is destroyed in one-half hour by a solution of  $\text{HgCl}$  1 to 6,000, while in blood serum 1 to 800 was required to destroy it in the same time. These

facts make our local treatment by antiseptics absolutely worthless and teach us that our raid on the bacilli by these means is all in vain. As far as gargling, spraying and insufflating are concerned I think it impossible to reach the bacilli by these manipulations; even if it were possible the effect of the antiseptic would be of too short a duration to destroy the germ. Still I use gargling and spraying (merely with pure water) not to affect the bacilli but only for cleansing purposes and as a tonic to stimulate the circulation in the fauces. The other two manipulations, swabbing and cauterizing with antiseptics, astringents, etc., oppose the first law in the treatment of acute diseases, viz., to give absolute rest to the diseased organ. Instead of doing so we keep up a continual irritation and congestion to the locus morbi. Furthermore I think it entirely wrong to remove the diphtheritic membrane which is only the local manifestation of general toxemia. That the membrane is an inseparable factor of the process of the disease, although there is no satisfactory explanation for its existence, we see from the fact that as long as the fever and the general symptoms exist, it quickly returns when removed, while after their disappearance the dissolution of the membrane quickly follows. So it appears to me that our local treatment as such is merely illusory and valueless; it is based upon theoretical principles which are derived from experiments on bacterial cultures and which can never be carried out in practice. But the local treatment is not only worthless in itself, but very harmful otherwise. I have already mentioned the harm done by the continual irritation and congestion caused by swabbing and cauterizing, the removal of the membrane and the destroying of the tissue. Furthermore we must consider that a part of the applied solution is always swallowed and absorbed into the system. And will we say that these drugs after having been absorbed do not cause toxic effects before we can ascertain these from outward appearances? But even if the drugs



did not produce any direct toxic effects, they would disturb the natural healing process which represents those complex symptoms we generally call disease. They must be eliminated from our system, and this elimination depends in the last instance upon the vital energy which at the same time is engaged in overcoming the disease and in eliminating the products of the same. And it depends upon the severity of the infection and the amount of vital power the body possesses, whether the patient recovers in spite of the two-fold demand or if he succumbs, because his vital energy was not sufficient to cope with both disease and drugs. I need not say that I think the internal medication with antiseptics such as chlorate of potassium and the like just as injurious and illusory as the local treatment, for we will never succeed in making the blood an antiseptic solution to kill the bacillus or its products without destroying the blood itself. As great as the discovery of external antiseptics is, there will never be an internal antiseptics, and the sooner we entertain this idea, the better for ourselves and our patients. Why I discredit those other drugs we use for internal medication, such as sesquichlorid of iron, tincture of iodine and others, I will explain more elaborately in a future article in which I will state my position concerning the drug treatment in general.

I still maintain that the drug treatment in diphtheria is merely imaginary and only produces ill effects which undoubtedly have a great influence upon the mortality and the course of the disease. And I do not see why the exclusion, even if only partial, of this treatment shall not give better results than we obtained before. The better results with the present treatment of typhoid for instance, are also not due exclusively to the hygienic treatment, but in a great measure to the exclusion of the drug treatment.

As long as no extensive investigations have been made into the combined drug and antitoxin treatment of diphtheria, my assertion that the exclusion of drugs is partially accountable for the better results, is

not contradicted. Whoever has had sufficient experience with physiologic therapy, will not at all be surprised at the lower mortality which is claimed for the antitoxin after excluding the drugs. He will only be surprised that not more patients died from diphtheria under the old drug poisoning, a treatment which evinced the wonderful capacity the vital power possesses and which showed how much a human being can endure.

In regard to the third statement I do not doubt a moment that many physicians have seen very favorable changes in the course of the disease under the antitoxin treatment, and I believe that such favorable changes lead more physicians to become followers of the antitoxin treatment than the statistics do. But the question is: Are these changes, even could we exclude endemic and epidemic conditions, to be ascribed exclusively to the serum? If we leave nature alone and do not disturb her wise provisions by applying drugs, the good results of which are merely imaginary and which only manifest toxic effects upon the system, we can see many most remarkable changes in the course of the disease, changes which we formerly made impossible by our drug treatment, and which we therefore can accomplish more readily by substituting the less harmful antitoxin.

It is surprising to note what great effect any such unexpected favorable change has upon the medical attendant. I know physicians who were opposed to the serum treatment, but who became most enthusiastic promoters of it, having injected antitoxin in but one or two cases in which they could observe some improvement afterward. If, however, a physician once believes in the efficacy of the serum, he will meet with enough cases in which he can find some advantageous changes, such as decrease in temperature, improved general condition, more rapid dissolution of the membrane, and so on, which he can ascribe to it. Any other less harmful treatment, if used in every acute disease of which fever is a pronounced symp-

tom, would show the same efficaciousness as the serum treatment for diphtheria does to-day.

It would be a thousand times better to pay more attention to those cases in which the antitoxin failed to succeed than to be so much enthused over those showing some good results which are merely incidental in many instances. We can not sustain the infallibility of the serum-therapy in those cases which terminate in death, by saying that death was due to a mixed infection, or that the cases did not come under treatment early enough. The latter excuse, it appears to me, is made too often, and not always in a very logical way. If we inject antitoxin into a child who perhaps was sick for four or five days, and this child dies, the treatment came too late, while if it recovers we are surprised at the wonderful efficacy of the remedy. I think this is a very illogic way of reasoning. If no fatally ending case injected on the fourth or fifth day proves anything against the antitoxin, no case which recovers, under the same conditions, is proof of the efficacy of the remedy. Beside, it is not at all proven that the antitoxin is an almost sure cure when injected the first day, as some enthusiasts claim. We can corroborate this by numerous reports, for instance: Dr. J. Winters, in the *New York Medical Journal* of Feb. 15, 1896, states that in the Willard Parker Hospital, in 1895, they injected antitoxin on the first day of the disease into 108 children with a mortality of 10.09 per cent.

Furthermore, most of what has been claimed for the antitoxin as, for instance, decrease in temperature, improvement in the general condition, more rapid dissolution of the membrane, and so on, has already been abandoned. I refer again to the report of Dr. Winters, stating that in the Willard Parker Hospital in April, 1895, it was left to the patients, respectively their parents, to decide whether antitoxin should be used or not. Those cases which were not treated with serum proved to take just as good a course, if not a better one, as those in which antitoxin was used. A

similar report is made by Prof. Soerensen of Copenhagen (*Therapeutische Monatshefte*, March, 1896).

As far as the fourth statement is concerned, I consider the serum-therapy less harmful than the former drug treatment; still its employment does not seem to be altogether devoid of danger. I only wish to call attention to the very valuable investigations of Dr. James Ewing, who found that the antitoxin caused a diminution of the red blood corpuscles and extensive changes in the leucocytes, and he concludes that these changes are likely to lead to obstructions in the capillary circulation, to changes in the kidneys, to necrotic foci in the liver, to pneumonia areas in the lungs, to obstructions of the cerebral circulation and possibly to convulsions.

In regard to the fifth statement I doubt whether our short experience of only two years is sufficient to decide the value of the serum treatment in membranous croup, as the type of laryngeal diphtheria varies too much. In some epidemics almost every case of croup ends in recovery, while in others most of the cases terminate in death. A severe epidemic may teach us quite different from what we believe to-day. That the praise of antitoxin, as far as its use in croup is concerned, is not so unanimous as is claimed, we see from numerous reports. Vierordt, for instance, claims a mortality of 40 per cent. under the serum treatment.

Beside, it is difficult to understand what effect the antitoxin should have in a case of diphtheria in which the general symptoms scarcely attract our attention and in which the localization of the membrane and the mechanical occlusion of the glottis are the only danger. And also I do not understand why the antitoxin should be timely enough in croup, a diphtheria which perhaps existed four or five days or longer, while in other cases we require the antitoxin to be injected on the first or second day in order to be of benefit to the patient. By the way, I believe there are quite a number of cases diagnosed as membranous



croup which in fact are but catarrhal croup, because it usually is impossible to make a laryngoscopic examination in a child. Even if the patient shows diphtheritic membranes on the tonsils a croup can be spasmodic. I lately was called to a 12 year old boy who showed a slight rise in temperature, severe general symptoms, swelling of the maxillary glands, a small membranous spot on the left tonsil and an "exquisite" croupy cough. The parents requested me to use antitoxin, which I declined. I made a laryngoscopic examination and convinced myself that the boy had no diphtheritic but only catarrhal croup. Had the case concerned a younger child in which a laryngoscopic examination had been impossible, and had I used antitoxin, I would have taken the case to be membranous croup and would have ascribed the recovery to the influence of the serum. But even if a physician had the opportunity to employ the antitoxin in a large number of cases of croup during a longer period and in different epidemics, I would not summarily ascribe his better results to the serum, unless I would know the kind of treatment he formerly employed and now excludes under the serum treatment.

I do not see why the dissolution of the membrane in the larynx, which is only a part of the whole healing process, should not be benefited by the exclusion of the drugs just as much as the dissolution of the membrane in the pharynx does.

I finally wish to call attention to the report of Bertin (*Gazette médicale de Nantes*, 1895, No. 4), who used plain horse serum in three cases of membranous croup, all recovering which leads me to believe that antitoxin is not a specific. These cases were as follows: 1. Five year old girl. Diphtheria of pharynx; membranous croup; swelling of the maxillary glands; Löffler bacillus found; 20 c.cm. of not immunized horse serum injected on the third day of the disease. Rapid improvement. On the sixth day all symptoms have disappeared. On the ninth day severe urticaria

over the whole body which heals gradually. 2. Nineteen year old girl. Diphtheria of pharynx; membranous croup; swelling of the maxillary glands; Löffler bacillus found. On the second day 20 c.cm. of not immunized horse serum injected. On the following day peeling off of large pieces of the membrane. Urticaria and alarming general symptoms. Complete recovery twenty-two days after the onset of the disease. 3. Four year old boy. Croup and symptoms of suffocation; Löffler bacillus found. In the evening of the second day 16 c.cm. of not immunized horse serum injected. Great improvement the following day. Complete recovery in the course of four days. Urticaria after another week.

As to the sixth statement, I can only say that Dr. X.'s experience is different from mine. I do not say, *deny* of course, that there are instances in which most of the members of a family get infected from a case of diphtheria. But looking over my experience, and I judge from this only, I must say that extensive contagion occurred but in the minority of my cases. To show that I am not isolated in my opinion I wish to call attention to a very instructive treatise (Bacteriological Investigations of Diphtheria in the United States) by Dr. Wm. Welch, Professor of Pathology at the Johns Hopkins University, which appeared in the *American Journal of the Medical Sciences*, October, 1894. Welch found in a group of 113 cases of pseudo-diphtheria (which differs from true diphtheria only by absence of the Löffler bacillus) occurring in 100 different families, that only in nine families the disease affected more than one member, and in a group of 70 cases of true diphtheria occurring in 50 different families, in only 13 families was more than one member affected.

The question whether the immunizations have such a great prophylactic value as is claimed, is, it seems to me, not yet settled. Hilbert, who favors the prophylactic use of antitoxin, states that in 64 children whom he immunized, he saw "but" 7 infections.

which equals 11 per cent. To judge from my own experience I hardly think that in more than 11 per cent. of my cases contagion took place without immunization. But even if the antitoxin had an immunizing effect, this effect would be of short duration only and might do more harm than good. It does not appear to me that the large dose of carbolic acid injected with the serum, should be so indifferent. It also seems very peculiar to think that an agent which, like the antitoxin, is said to possess the power of neutralizing such a pernicious poison as the toxins of diphtheria are, should be so harmless.

Concerning the seventh and last statement, I firmly believe that for typhoid we will never have a serum-therapy which will amount to very much, because typhoid runs a more regular course than diphtheria does, so that we do not come in contact with so many unexpected favorable changes as we do in the latter disease. Still, very industrious efforts have been and are being made to discover an antitoxin for typhoid; I only refer to Fränkel, who has largely experimented for this purpose. Lately Dr. Klemperer of Strassburg thinks he has discovered an antitoxin against typhoid and has made experiments with it on dogs. He even employed it on five patients, and is of the opinion that he obtained a good result in so far as the disease took a mild course (*Berliner Medizinische Wochenschrift*, 1895, No. 28). But in spite of these industrious investigations, I do not believe that there will ever be a serum-therapy for typhoid which will be superior to the hydropathic treatment, as far as the mortality, the course of the disease and the *restitutio ad integrum* are concerned.

What I have said in the foregoing lines is, of course, only my personal view of the matter. If I should be mistaken in every or any part, I would be thankful to have some one refute my assertions. The subject is of such great importance that it ought to be discussed from every possible standpoint, and whosoever is opposed to the serum treatment, no matter what his

reasons may be, should come forward and proclaim himself, though he may not receive the attention paid those who boast of the wonderful efficacy of the new remedy, an efficacy for which they have no more scientific proof than they have for the efficacy of most of the drugs. What do we know of the antitoxin and its action? Nothing. Nobody knows what antitoxin is. For what does it matter, if we are told that "the antitoxins are products of bacteria formed in the blood of the animal body, though we do not know the process of the formation of these antitoxins and their chemie nature," or if, as Roux believes, "the antitoxins are produced by cells, but not by the white blood corpuseles." Similar philosophic explanations are given in regard to the action of the antitoxin, but of what benefit is it if, as Roux believes, "the injection of antitoxin will not cause neutralization of the bacterial poison, but a rapid process of immunizing." Another explanation, for which we hardly can give any positive proof, is that of Pohl. Pohl says "the greatest part of the albumin in the alimentary canal is transformed into lymph cells inside the lymphatic tissues of the intestinal wall; that means it is organized into a living form of albumin. Those leucocytes which have been so formed in the intestinal walls are thrown into the circulation and perish inside of the circulatory channels and in the tissues. So that a few hours after each meal active albumin will be present in solution in the blood. If now we inject into rabbits or sheep pure cultures of erysipelas, for instance, the streptococci will perish in the animal body in great numbers, and it is very probable that the albuminous part of their bodies will combine with the active blood albumin, the immune protein, and form immune proteidin which kills anthrax bacilli."

Others claim that the antitoxin causes an increased leucocytosis, but this explanation is also objectionable. We know that leucocytosis in an acute disease sets in only after the acute stage is passed, a fact which proves with undoubted certainty that it dare



not set in before. If we, therefore, should succeed in producing it at an earlier stage, we would disturb the healing process in which every single cell has its definite place and time and function. Again, others explain the effects of the antitoxin by the amount of carbolic acid injected with the serum.

It is also claimed that there is nothing specific in the diphtheria antitoxin, but that it only produces a stronger reaction. This idea seems to be supported by Bertin, who had good results with non-immunized horse serum, and by Emmerich, who reports excellent effects in diphtheria from injections of erysipelas antitoxin.

To judge from my experience, I think there is nothing which can equal the physiologic treatment in producing a powerful reaction which, by the way, is superior to the one caused by the antitoxin, inasmuch as no ill effects are produced, as is the case in the serum treatment.

The serum-therapy stands on the same footing as the drug treatment, being only a matter of belief, and as long as a physician believes in the latter, he can not be blamed for believing in the former. But those practitioners are to be blamed who in their enthusiasm go so far as to call other physicians criminal, because these do not follow their way of jumping at any new treatment which is presented. The day will come when this order of things will be reversed, and those using the serum treatment will be placed in the same light as those not using it to-day. And the adroitness with which those enthusiasts of to-day will extricate themselves from the affair will only be equaled by the facility with which they will take up the next fad that comes along. If there were a hundred diseases which could be treated on the principle of the serum-therapy, and in ninety-nine this treatment would prove to be a failure, there would yet be physicians who would try it in the hundredth, although their experience in the other ninety-nine diseases should have taught them that the system they followed was erroneous.

The serum-therapy will undoubtedly be the prevail-

ing treatment in diphtheria for a long time, because it is used in an acute disease in which any treatment has a good chance, especially if it is much less harmful than the drug treatment. The serum treatments we have had and will have in chronic diseases, will only be of short duration. But also the antitoxin treatment of diphtheria will not last forever. Some severe epidemic may occur in which the diphtheria antitoxin, alone or in conjunction with the streptococcus antitoxin, will be found wanting in spite of a timely employment. And then it will go the same way the other inoculations and vaccinations for syphilis, anthrax, cholera, hydrophobia and tuberculosis went. Yet I want to say that I am far from thinking that those industrious investigations which have been and are being made concerning the serum-therapy, are in vain. On the contrary, they will be of great benefit to mankind, for they will finally convince us that we can not rely upon the blood serum of a horse or any other animal, not even on that of another man, but only upon our own individual serum.

And they will teach us that only by a hygienic way of living can we immunize ourselves; that means, improve the physiologic functions of our body and the bactericide power of our blood. They will also teach us that in diseases we can rely upon the same agents only, on which natural immunization is based and of which physiologic treatment consists.

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